CLAIM LISTING

This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (Currently amended) A method of modulating the expression of a target RNA molecule in a eukaryotic cell comprising the step of contacting the cell with an oligonucleotide consisting of 8 to 80 linked nucleosides and having

    a) a first region of nucleotides, each having a first conformation which, when the oligonucleotide is bound to the target RNA molecule, forms a substrate for cleavage by an RNase;

    b) a second region of nucleotides, each having a second conformation which, when the oligonucleotide is bound to the target RNA molecule does not form a substrate for cleavage by an RNase, and

    c) a transition moiety positioned between the first and the second regions which modulates the transmission of the conformation of the second region into the first region, wherein the transition moiety comprises at least one modified nucleotide that does not form hydrogen bonds with the target RNA molecule.

2. (Original) The method of claim 1, wherein the second region is positioned 5' to the first region.

3. (Original) The method of claim 1, wherein the first region comprises deoxynucleotides.

4. (Original) The method of claims 3, wherein the second region comprises 2'-O-alkoxyalkyl ribonucleotides.

5. (Original) The method of claim 4, wherein the 2'-O-alkoxyalkyl ribonucleotides are 2'-O-methoxyethyl ribonucleotides.

6. (Original) The method of claim 1, wherein the internucleotide linkages in the first or second regions are phosphorothioates.

7. (Canceled)

8. (Canceled)

9. (Previously presented) The method of claim 1, wherein the modified nucleotide is selected from a modified base nucleotide, a modified sugar nucleotide, a modified or unmodified sugar abasic nucleotide, a THF nucleotide, or an acyclic nucleotide.

10. (Canceled)

11. (Previously presented) The method of claim 1, wherein the modified nucleotide comprises a modified base moiety capable of π stacking with adjacent bases.

12. (Original) The method of claim 11, wherein the modified base moiety is a universal base, a promiscuous base, a size expanded base or a fluorinated base.

13. (Original) The method of claim 12, wherein the modified base moiety is tetrafluoroindolyl.

14. (Previously presented) The method of claim 9, wherein the modified sugar nucleotide is a 2'-ara-modified nucleotide.

15. (Original) The method of claim 14, wherein the 2'-ara-modified nucleotide is a 2'-ara-fluoro nucleotide.

16. (Previously presented) The method of claim 9, wherein the modified sugar moiety is an acyclic sugar analog.

17. (Previously presented) The method of claim 1, further comprising a third region of nucleotides, each having a third conformation which, when the oligonucleotide is bound to the target RNA molecule does not form a substrate for cleavage by an RNase.

18. (Canceled)

19. (Previously presented) The method of claim 17, wherein the third region has the same conformation as the second region.

20. (Original) The method of claims 19, wherein the second region comprises 2'-O-alkoxyalkyl ribonucleotides.

21. (Original) The method of claim 20, wherein the 2'-O-alkoxyalkyl ribonucleotides are 2'-O-methoxyethyl ribonucleotides.

22. (Previously presented) The method of claim 17, comprising a second transition moiety which modulates the transmission of the conformation of the third region into the first region, and wherein the second transition moiety comprises at least one modified nucleotide that does not form hydrogen bonds with the target RNA molecule.

23. (Canceled)

24. (Previously presented) The method of claim 22, wherein the modified nucleotide of the second transition moiety is selected from a modified base nucleotide, a modified sugar nucleotide, a modified or unmodified sugar abasic nucleotide, a THF nucleotide, or an acyclic nucleotide.

25. (Canceled)

26. (Previously presented) The method of claim 24, wherein the modified base nucleotide of the second transition moiety comprises a modified base moiety capable of π stacking with adjacent bases.

27. (Currently amended) The method of claim [[25]]26, wherein the modified base moiety of the second transition moiety is a universal base, a promiscuous base, a size expanded base or a fluorinated base.

28. (Currently amended) The method of claim [[25]]27, wherein the modified base moiety of the second transition moiety is tetrafluoroindolyl.

29. (Previously presented) The method of claim 24, wherein the modified sugar nucleotide of the second transition moiety is a 2'-ara-modified nucleotide.

30. (Previously presented) The method of claim 29, wherein the 2'-ara-modified nucleotide of the second transition moiety is a 2'-ara-fluoro nucleotide.

31. (Previously presented) The method of claim 24, wherein the modified sugar moiety of the second transition moiety is an acyclic sugar analog.

32. (Previously presented) The method of claim 1, wherein the eukaryotic cell is in an animal.